

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

**In re application of:** Lorens et al.

**Application No.** 10/696,909

**Filed:** October 29, 2003

**Confirmation No.** 9257

**For:** MODULATORS OF ANGIOGENESIS  
AND TUMORIGENESIS

**Examiner:** Peter J. Reddig

**Art Unit:** 1642

**Attorney Reference No.** 7946-79836-01

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**REPLY BRIEF**

This Reply Brief, filed in accordance with 37 C.F.R. § 41.41, responds to the Examiner's Answer dated February 2, 2009. A two-month period for response was set, making a reply due by **April 2, 2009**. This Reply Brief is considered to supplement the existing Appeal Brief filed by Appellants on November 21, 2008. All previous arguments presented in Appellants' Appeal Brief continue to be applicable and asserted in this Appeal.

**Grounds of Rejection to be Reviewed on Appeal**

Claims 1, 12, 14-18, 27, 41-44, and 54-61 are pending. Claims 1, 14, 27, 54-56, and 61 are rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Healy *et al.* (*Am. J. Physiol.* 280:L1273-1281, 2001). Claims 12, 15-18, 41-44, and 57-60 are rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Healy *et al.* in view of Varner and Cheresch (*Curr. Opin. Cell Biol.* 8:724-730, 1996), in further view of Ruoslahti *et al.* (U.S. Pat. No. 6,180,084), in further view of Panzer *et al.* (U.S. Pat. Publication No. 2004/0048253), and in further view of Klinghoffer *et al.* (U.S. Pat. Publication No. 2004/0077574).

### Reply to Examiner's Answer

#### A. *Rejection under 35 U.S.C. § 102(b)*

In the Examiner's Answer, the Office maintains that claims 1, 14, 27, 54-56, and 61 are anticipated under 35 U.S.C. § 102(b) by Healy *et al.* (*Am. J. Physiol.* 280:L1273-1281, 2001). The Office continues to allege that Healy *et al.* teach determining the *in vitro* kinase activity of an Axl polypeptide and performing a cell-based assay on cells that express Axl (including cell number and apoptosis) and thus inherently disclose a method for identifying a compound that inhibits angiogenesis. Appellants have previously argued that Healy *et al.* do not teach a method of identifying an *inhibitor* of angiogenesis; those arguments are reasserted herein.

For each of the rejections under 35 U.S.C. § 102(b) (*i.e.*, claims 1, 14, 54, and 55; claims 27 and 54; and claims 56 and 61), the Office asserts that the identification of an inhibitor of angiogenesis is merely an intended result expressed in the preamble and the wherein clause of each independent claim (claims 1, 27, and 56). The Office states that a "wherein clause in a method claim is not given weight when it simply expresses the intended result of a process step positively recited..." (Examiner's Answer, page 4, third paragraph). With respect to this rejection, the Office also states that the "recitation of identifying a compound that inhibits angiogenesis has not been given patentable weight because the recitation occurs in the preamble" (Examiner's Answer, paragraph bridging pages 11-12). Appellants disagree with the assertions that the preamble and the wherein clause of the pending claims should not be given patentable weight.

#### Preamble

Each of the independent claims (claims 1, 27, and 56) has a preamble reciting a "method for identifying a compound that inhibits angiogenesis..." The Office states that the preamble of the independent claims is not given patentable weight, because a preamble "is generally not accorded any patentable weight where it merely recites the purpose of a process...and where the body of the claim does not depend on the preamble for completeness..." (Examiner's Answer, page 12, lines 1-3).

Appellants respectfully point out that whether the preamble of a claim is a limitation (*i.e.*, is given patentable weight) is determined on a case by case (and claim by claim) basis. “Whether a preamble stating the purpose and context of the invention constitutes a limit of the claimed process is determined on the facts of each case in light of the overall form of the claim, and the invention as described in the specification and illuminated in the prosecution history.” *Applied Materials, Inc. v. Advanced Semiconductor Materials Am., Inc.* 98 F.3d 1563, 1572-73, 40 USPQ2d 1481, 1488 (Fed. Cir. 1996). The Federal Circuit defined several situations in which a preamble may limit claim scope in *Catalina Marketing Int’l, Inc. v. Coolsavings.com, Inc.* 289 F.3d 801, 808, 62 USPQ2d 1781, 1785 (Fed. Cir. 1995). In one example, “clear reliance on the preamble during prosecution to distinguish the claimed invention from the prior art transforms the preamble into a claim limitation because such reliance indicates use of the preamble to define, in part, the claimed invention.” *Id.* F.3d at 808, USPQ2d at 1785.

Under the controlling law, the preamble must be given patentable weight in the present claims, as there has been clear reliance on the preamble to distinguish the claimed invention from Healy *et al.* throughout the prosecution history. The preambles of claims 1 and 27 were amended to recite a “method for identifying a compound that inhibits angiogenesis” in the amendment submitted February 23, 2007, in response to the first Non-final Office action of August 23, 2006 (claim 56 was not added until March 12, 2008). In response to the rejection of the claims under 35 U.S.C. § 102(b), Appellants argued that “Healy *et al.* does not disclose identification of an inhibitor of angiogenesis using the Axl polypeptide and cannot anticipate the claims.” Amendment and Response of February 23, 2007, page 15, third paragraph. Appellants continued to assert this same argument in subsequent responses to Office actions that alleged anticipation in light of Healy *et al.* (*e.g.*, response of October 5, 2007, page 11, first full paragraph; response of September 23, 2008, page 13, first full paragraph). The prosecution history reflects that Appellants amended the preamble to distinguish the claims from Healy *et al.* and have clearly relied on the preamble during prosecution. Therefore, the preamble must be given patentable weight.

### Wherein Clause

Each of the independent claims (claims 1, 27, and 56) ends with a wherein clause reciting “wherein inhibition of [the kinase activity and/or the angiogenesis phenotype] in the presence of the compound identifies the compound as a compound that inhibits angiogenesis.” The Office states that a “wherein clause in a method claim is not given weight when it simply expresses the intended result of a process step positively recited...” (Examiner’s Answer, page 12, first paragraph).

Appellants first point out that the MPEP states that the determination of whether a wherein clause is a claim limitation “depends on the specific facts of the case” (MPEP § 2111.04). When the wherein clause “states a condition that is material to patentability, it cannot be ignored in order to change the substance of the invention.” *Hoffer v. Microsoft Corp.* 405 F.3d 1326, 1329, 74 USPQ2d 1481, 1483 (Fed. Cir. 2005). In *Hoffer*, the whereby clause described a network of users at remote terminals who are able to engage in interactive data messaging. The court held that this was more than an intended result, and was “described in the specification and prosecution as an *integral part* of the invention.” *Hoffer* F.3d at 1330, USPQ2d at 1484 (emphasis added).

The wherein clause in claims 1, 27, and 56 states an integral part of the invention, and must be given patentable weight. As discussed above, the claims are clearly directed to a method of identifying an inhibitor of angiogenesis. The claims include assaying kinase activity of Axl polypeptide (claims 1 and 56) and/or performing a cell-based assay which produces an angiogenesis phenotype (claims 1 and 27). However, in order to achieve the claimed invention, one must determine whether the tested compound is an inhibitor of angiogenesis (as opposed to a compound that has no effect on angiogenesis or stimulates angiogenesis). This determination is expressed in the wherein clause, such that if the compound inhibits the kinase activity and/or the angiogenesis phenotype in the cell-based assay, then the compound is identified as an inhibitor of angiogenesis (see, e.g., specification at page 9, lines 16-22; page 30, lines 6-10). Without the wherein clause, one does not in fact achieve the identification of a compound that inhibits angiogenesis. Rather, at most, one identifies a compound that has some effect on Axl kinase

activity and/or a cell-based angiogenesis phenotype. Thus, the wherein clause must be given patentable weight.

### Summary

At least for the reasons discussed above, both the preamble and the wherein clause of independent claims 1, 27, and 56 must be given patentable weight. Appellants reassert the arguments previously presented in the Appeal Brief submitted on November 21, 2008 that Healy *et al.* do not expressly or inherently teach the claimed method of identifying a compound that is an inhibitor of angiogenesis. Thus, Appellants respectfully request that the rejection of claims 1, 14, 27, 54-56, and 61 under 35 U.S.C. § 102(b) be reversed.

### ***B. Rejection under 35 U.S.C. § 103(a)***

Claims 12, 15-18, 41-44, and 57-60 remain rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Healy *et al.* in view of Varner and Cheresch (*Curr. Opin. Cell Biol.* 8:724-730, 1996), in further view of Ruoslahti *et al.* (U.S. Pat. No. 6,180,084), in further view of Panzer *et al.* (U.S. Pat. Publication No. 2004/0048253), and in further view of Klinghoffer *et al.* (U.S. Pat. Publication No. 2004/0077574).

To establish a *prima facie* case of obviousness, the Office must show that the references teach or suggest all claim limitations. “When determining whether a claim is obvious, an Examiner must make ‘a searching comparison of the claimed invention – *including all its limitations* – with the teaching of the prior art.’ Thus, ‘obviousness requires a suggestion of all limitations in a claim.’” *Ex parte Mumper* BPAI, Appeal No. 2008-2332, June 27, 2008.

Claims 12 and 15-18 depend from claim 1, claims 41-44 depend from claim 27, and claims 57-60 depend from claim 56. At least for the reasons discussed above, Healy *et al.* do not teach all the limitations of the independent claims (claims 1, 27, and 56), namely, Healy *et al.* do not teach or even suggest identification of an inhibitor of angiogenesis. The Office asserts that Healy *et al.* disclose that apoptosis has a role in vascular remodeling associated with tumor angiogenesis and show that Axl activity has a role in endothelial cell survival, and thus one of skill in the art would be motivated to study the effects of various compounds on Axl kinase

activity and endothelial cell survival (Examiner's Answer, page 18, paragraph 2). Appellants note that the Office has provided no evidence as to what role apoptosis has in tumor vascular remodeling and Appellants assert that based on Healy *et al.* one of skill in the art would have had no reasonable expectation that an inhibitor of Axl kinase activity or a cell-based angiogenesis assay would be an inhibitor of angiogenesis.

Appellants reassert the arguments previously presented in the Appeal Brief submitted on November 21, 2008 that none of the additional references (Varner and Cheresch, Ruoslahti *et al.*, Panzer *et al.*, or Klinghoffer *et al.*) cure this deficiency of Healy *et al.* Therefore, a *prima facie* case of obviousness is not supported and Appellants respectfully request that the rejection of claims 12, 15, 41-44, and 57-60 be reversed.

### Conclusion

Appellants submit that the rejections under 35 U.S.C. § 102 and 35 U.S.C. § 103 should be reversed, and respectfully request the allowance of the pending claims.

Respectfully submitted,

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